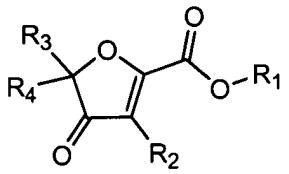
Listing of the Claims

Please cancel claim 6 and amend claims 1, 7, 8 and 21 as follows. This listing of claims replaces all prior versions and listings of claims in the application.

1. (currently amended) A compound of Formula (**I**):



(**I**)

or a pharmaceutically acceptable salt, hydrate or solvate thereof,

wherein:

R_1 is H or C_{1-6} alkyl;

R_2 is H, halogen, C_{1-4} alkyl or C_{1-4} haloalkyl; and

A) R_3 is aryl, C_{3-7} cycloalkyl, C_{3-7} cycloalkenyl, heteroaryl, C_{3-7} heterocycloalkyl or C_{3-7} heterocycloalkenyl wherein each are optionally substituted with 1 to 5 substituents selected from the group consisting of C_{1-6} acyloxy, C_{2-6} alkenyl, C_{1-6} alkoxy, C_{1-6} alkyl, C_{1-6} alkylcarboxamide, C_{2-6} alkynyl, C_{1-6} alkylsulfonamide, C_{1-6} alkylsulfinyl, C_{1-6} alkylsulfonyl, C_{1-6} alkylthio, C_{1-6} alkylureyl, C_{1-6} alkylamino, amino, aryl, substituted aryl, carbo-C_{1-6}-alkoxy, carboxamide, cyano, C_{3-7} cycloalkyl, C_{2-6} dialkylamino, C_{2-6} dialkylcarboxamide, C_{2-6} dialkylsulfonamide, halogen, C_{1-6} haloalkoxy, C_{1-6} haloalkyl, C_{1-6} haloalkylsulfinyl, C_{1-6} haloalkylsulfonyl, C_{1-6} haloalkylthio, heteroaryl, substituted heteroaryl, hydroxyl, nitro and thiol; and

R_4 is selected from the group consisting of H, ethyl, ~~n-propyl,~~ C_{4-6} alkyl and C_{1-6} haloalkyl wherein each are optionally substituted with 1 to 5 substituents selected from the group consisting of C_{1-6} acyloxy, C_{2-6} alkenyl, C_{1-6} alkoxy, C_{1-6} alkylcarboxamide, C_{2-6} alkynyl, C_{1-6} alkylsulfonamide, C_{1-6} alkylsulfinyl, C_{1-6} alkylsulfonyl, C_{1-6} alkylthio, C_{1-6} alkylureyl, C_{1-6} alkylamino, amino, carbo-C_{1-6}-alkoxy, carboxamide, cyano, C_{3-7} cycloalkyl, C_{2-6} dialkylamino, C_{2-6} dialkylcarboxamide, C_{2-6} dialkylsulfonamide, halogen, C_{1-6} haloalkoxy, C_{1-6} haloalkyl, C_{1-6} haloalkylsulfinyl, C_{1-6} haloalkylsulfonyl, C_{1-6} haloalkylthio, hydroxyl, nitro and thiol; or

R_4 is C_{3-6}-cycloalkyl optionally substituted with 1 to 5 substituents selected from the group consisting of C_{1-6} acyloxy, C_{2-6} alkenyl, C_{1-6} alkoxy, C_{1-6} alkyl, C_{1-6} alkylcarboxamide,

C_{2-6} alkynyl, C_{1-6} alkylsulfonamide, C_{1-6} alkylsulfinyl, C_{1-6} alkylsulfonyl, C_{1-6} alkylthio, C_{1-6} alkylureyl, C_{1-6} alkylamino, amino, carbo-C_{1-6}-alkoxy, carboxamide, cyano, C_{3-7} cycloalkyl, C_{2-6} dialkylamino, C_{2-6} dialkylcarboxamide, C_{2-6} dialkylsulfonamide, halogen, C_{1-6} haloalkoxy, C_{1-6} haloalkyl, C_{1-6} haloalkylsulfinyl, C_{1-6} haloalkylsulfonyl, C_{1-6} haloalkylthio, hydroxyl, nitro and thiol; or

B) R_3 is a substituted phenyl, 2-chlorophenyl, 3-chlorophenyl, naphthyl, C_{3-7} cycloalkyl, C_{3-7} cycloalkenyl, heteroaryl, C_{3-7} heterocycloalkyl or C_{3-7} heterocycloalkenyl wherein said 2-chlorophenyl, 3-chlorophenyl, naphthyl, C_{3-7} cycloalkyl, C_{3-7} cycloalkenyl, heteroaryl, C_{3-7} heterocycloalkyl and C_{3-7} heterocycloalkenyl are optionally substituted with 1 to 5 substituents selected from the group consisting of C_{1-6} acyloxy, C_{2-6} alkenyl, C_{1-6} alkoxy, C_{1-6} alkyl, C_{1-6} alkylcarboxamide, C_{2-6} alkynyl, C_{1-6} alkylsulfonamide, C_{1-6} alkylsulfinyl, C_{1-6} alkylsulfonyl, C_{1-6} alkylthio, C_{1-6} alkylureyl, C_{1-6} alkylamino, amino, aryl, substituted aryl, carbo-C_{1-6}-alkoxy, carboxamide, cyano, C_{3-7} cycloalkyl, C_{2-6} dialkylamino, C_{2-6} dialkylcarboxamide, C_{2-6} dialkylsulfonamide, halogen, C_{1-6} haloalkoxy, C_{1-6} haloalkyl, C_{1-6} haloalkylsulfinyl, C_{1-6} haloalkylsulfonyl, C_{1-6} haloalkylthio, heteroaryl, substituted heteroaryl, hydroxyl, nitro and thiol; and wherein said substituted phenyl is substituted with 1 to 5 substituents selected from the group consisting of C_{1-6} acyloxy, C_{2-6} alkenyl, C_{1-6} alkoxy, C_{1-6} alkyl, C_{1-6} alkylcarboxamide, C_{2-6} alkynyl, C_{1-6} alkylsulfonamide, C_{1-6} alkylsulfinyl, C_{1-6} alkylsulfonyl, C_{1-6} alkylthio, C_{1-6} alkylureyl, C_{1-6} alkylamino, amino, aryl, substituted aryl, carbo-C_{1-6}-alkoxy, carboxamide, cyano, C_{3-7} cycloalkyl, C_{2-6} dialkylamino, C_{2-6} dialkylcarboxamide, C_{2-6} dialkylsulfonamide, F, Br, I, C_{1-6} haloalkoxy, C_{1-6} haloalkyl, C_{1-6} haloalkylsulfinyl, C_{1-6} haloalkylsulfonyl, C_{1-6} haloalkylthio, heteroaryl, substituted heteroaryl, hydroxyl, nitro and thiol; and

R_4 is selected from the group consisting of H, ~~C_{1-6} alkyl,~~ methyl, ethyl, C_{3-6}-cycloalkyl and C_{1-6} haloalkyl wherein each are optionally substituted with 1 to 5 substituents selected from the group consisting of C_{1-6} acyloxy, C_{2-6} alkenyl, ~~C_{1-6} alkoxy,~~ C_{1-6} alkyl, C_{1-6} alkylcarboxamide, C_{2-6} alkynyl, C_{1-6} alkylsulfonamide, C_{1-6} alkylsulfinyl, C_{1-6} alkylsulfonyl, C_{1-6} alkylthio, C_{1-6} alkylureyl, C_{1-6} alkylamino, amino, carbo-C_{1-6}-alkoxy, carboxamide, cyano, C_{3-7} cycloalkyl, C_{2-6} dialkylamino, C_{2-6} dialkylcarboxamide, C_{2-6} dialkylsulfonamide, halogen, C_{1-6} haloalkoxy, C_{1-6} haloalkyl, C_{1-6} haloalkylsulfinyl, C_{1-6} haloalkylsulfonyl, C_{1-6} haloalkylthio, hydroxyl, nitro and thiol.

2. (original) The compound according to claim 1 wherein R_1 is C_{1-6} alkyl.

3. (original) The compound according to claim 1 wherein R_1 is methyl or ethyl.

4. (original) The compound according to claim 1 wherein R_1 is H.

5. (previously presented) The compound according to claim 1 wherein R_2 is H.

6. (canceled)

7. (currently amended) The compound according to ~~claim 6~~ claim 1 wherein R_4 is methyl.

8. (currently amended) The compound according to ~~claim 6~~ claim 1 wherein R_4 is ethyl.

9. (previously presented) The compound according to claim 1 wherein R_4 is C_{1-6} haloalkyl.

10. (previously presented) The compound according to claim 9 wherein R_4 is trifluoromethyl.

11. (previously presented) The compound according to claim 1 wherein R_3 is substituted phenyl, 3-chlorophenyl, C_{3-7} cycloalkyl, C_{3-7} cycloalkenyl or heteroaryl, wherein said 3-chlorophenyl, C_{3-7} cycloalkyl, C_{3-7} cycloalkenyl and heteroaryl are optionally substituted with 1 to 5 substituents selected from the group consisting of C_{2-6} alkenyl, C_{1-6} alkoxy, C_{1-6} alkyl, aryl, cyano, halogen, C_{1-6} haloalkyl and heteroaryl.

12. (previously presented) The compound according to claim 1 wherein R_3 is thienyl optionally substituted with C_{1-6} alkyl, halogen or C_{1-6} haloalkyl.

13. (previously presented) The compound according to claim 1 wherein R_3 is thienyl optionally substituted with methyl, ethyl, F, Cl, Br, I or trifluoromethyl.

14. previously presented) The compound according to claim 1 wherein R_3 is selected from the group consisting of biphenyl-3-yl, 3-thiophen-2-yl-phenyl, 3-bromo-phenyl, 3-iodo-phenyl, 3-chloro-phenyl, 3-fluoro-phenyl, 3,5-difluoro-phenyl, m-tolyl, 3-ethyl-phenyl, 3-trifluoromethyl-

phenyl, 4-fluoro-phenyl, 2-fluoro-phenyl, 3,4-difluoro-phenyl, 2,4-difluoro-phenyl, 2,6-difluoro-phenyl, 2,5-dichloro-phenyl, 3-methoxy-phenyl, 3,5-dichloro-phenyl, 3-cyano-phenyl, 3-propenyl-phenyl, 3-hex-1-enyl-phenyl and 3-vinyl-phenyl.

15. (previously presented) The compound according to claim 1 wherein R_3 is selected from the group consisting of thiophen-3-yl, thiophen-2-yl, 4-bromo-thiophen-2-yl, 5-methyl-thiophen-2-yl, 5-chloro-thiophen-2-yl, 5-bromo-thiophen-3-yl, 5-chloro-thiophen-3-yl, 4-bromo-5-methyl-thiophen-2-yl, pyridin-3-yl, furan-2-yl, 4-methyl-thiophen-2-yl and 5-methyl-thiophen-3-yl.

16. (previously presented) The compound according to claim 1 wherein R_3 is selected from the group consisting of cyclohex-1-enyl, cyclopent-1-enyl and cyclopentyl.

17. (original) The compound according to claim 1 wherein:

R_1 is H;

R_2 is H;

R_4 is C_{1-6} alkyl or C_{1-6} haloalkyl; and

R_3 is substituted phenyl, 3-chlorophenyl, C_{3-7} cycloalkyl, C_{3-7} cycloalkenyl or heteroaryl, wherein said 3-chlorophenyl, C_{3-7} cycloalkyl, C_{3-7} cycloalkenyl and heteroaryl are optionally substituted with 1 to 5 substituents selected from the group consisting of C_{2-6} alkenyl, C_{1-6} alkoxy, C_{1-6} alkyl, aryl, cyano, halogen, C_{1-6} haloalkyl and heteroaryl.

18. (original) The compound according to claim 1 wherein:

R_1 is H;

R_2 is H;

R_4 is methyl, ethyl or trifluoromethyl; and

R_3 is selected from the group consisting of biphenyl-3-yl, 3-thiophen-2-yl-phenyl, 3-bromo-phenyl, 3-iodo-phenyl, 3-chloro-phenyl, 3-fluoro-phenyl, 3,5-difluoro-phenyl, m-tolyl, 3-ethyl-phenyl, 3-trifluoromethyl-phenyl, 3,4-difluoro-phenyl, 2,4-difluoro-phenyl, 2,6-difluoro-phenyl, 2,5-dichloro-phenyl, 3-methoxy-phenyl, 3,5-dichloro-phenyl, 3-cyano-phenyl, 3-propenyl-phenyl, 3-hex-1-enyl-phenyl and 3-vinyl-phenyl.

19. (original) The compound according to claim 1 wherein:

R_1 is H;

R_2 is H;

R_4 is methyl, ethyl or trifluoromethyl; and

R_3 is thienyl optionally substituted with C_{1-6} alkyl or halogen.

20. (original) The compound according to claim 1 wherein:

R_1 is H;

R_2 is H;

R_4 is methyl, ethyl or trifluoromethyl; and

R_3 is selected from the group consisting of thiophen-3-yl, thiophen-2-yl, 4-bromo-thiophen-2-yl, 5-methyl-thiophen-2-yl, 5-chloro-thiophen-2-yl, 5-bromo-thiophen-3-yl, 5-chloro-thiophen-3-yl, 4-bromo-5-methyl-thiophen-2-yl, pyridin-3-yl, furan-2-yl, 4-methyl-thiophen-2-yl and 5-methyl-thiophen-3-yl.

21. (original) The compound according to claim 1 selected from the group consisting of:

5-Cyclohex-1-enyl-5-methyl-4-oxo-4,5-dihydro-furan-2-carboxylic acid;

5-Methyl-4-oxo-5-thiophen-3-yl-4,5-dihydro-furan-2-carboxylic acid methyl ester;

5-Methyl-4-oxo-5-thiophen-2-yl-4,5-dihydro-furan-2-carboxylic acid methyl ester;

5-(4-Bromo-thiophen-2-yl)-5-methyl-4-oxo-4,5-dihydro-furan-2-carboxylic acid methyl ester;

5-(4-Bromo-thiophen-2-yl)-5-methyl-4-oxo-4,5-dihydro-furan-2-carboxylic acid;

5-Methyl-5-(5-methyl-thiophen-2-yl)-4-oxo-4,5-dihydro-furan-2-carboxylic acid methyl ester;

5-Methyl-5-(5-methyl-thiophen-2-yl)-4-oxo-4,5-dihydro-furan-2-carboxylic acid;

5-(5-Chloro-thiophen-2-yl)-5-methyl-4-oxo-4,5-dihydro-furan-2-carboxylic acid methyl ester;

5-Cyclopent-1-enyl-5-methyl-4-oxo-4,5-dihydro-furan-2-carboxylic acid;

5-Biphenyl-3-yl-5-methyl-4-oxo-4,5-dihydro-furan-2-carboxylic acid methyl ester;

5-Methyl-4-oxo-5-(3-thiophen-2-yl-phenyl)-4,5-dihydro-furan-2-carboxylic acid methyl ester;

5-(3-Bromo-phenyl)-5-methyl-4-oxo-4,5-dihydro-furan-2-carboxylic acid methyl ester;

5-(3-Bromo-phenyl)-5-methyl-4-oxo-4,5-dihydro-furan-2-carboxylic acid;

5-(3-Iodo-phenyl)-5-methyl-4-oxo-4,5-dihydro-furan-2-carboxylic acid;
5-(3-Chloro-phenyl)-5-methyl-4-oxo-4,5-dihydro-furan-2-carboxylic acid;
5-(3-Fluoro-phenyl)-5-methyl-4-oxo-4,5-dihydro-furan-2-carboxylic acid;
5-(3,5-Difluoro-phenyl)-5-methyl-4-oxo-4,5-dihydro-furan-2-carboxylic acid;
5-Methyl-4-oxo-5-m-tolyl-4,5-dihydro-furan-2-carboxylic acid;
5-(3-Ethyl-phenyl)-5-methyl-4-oxo-4,5-dihydro-furan-2-carboxylic acid;
5-Methyl-4-oxo-5-(3-trifluoromethyl-phenyl)-4,5-dihydro-furan-2-carboxylic acid;
5-(5-Chloro-thiophen-2-yl)-5-methyl-4-oxo-4,5-dihydro-furan-2-carboxylic acid; and
5-Methyl-4-oxo-5-thiophen-2-yl-4,5-dihydro-furan-2-carboxylic acid; or
a pharmaceutically acceptable salt, hydrate or solvate thereof.

22. (original) The compound according to claim 1 selected from the group consisting of:
5-(5-Bromo-thiophen-3-yl)-5-methyl-4-oxo-4,5-dihydro-furan-2-carboxylic acid methyl ester;
5-(5-Bromo-thiophen-3-yl)-5-methyl-4-oxo-4,5-dihydro-furan-2-carboxylic acid;
5-(5-Chloro-thiophen-3-yl)-5-methyl-4-oxo-4,5-dihydro-furan-2-carboxylic acid methyl ester;
5-(5-Chloro-thiophen-3-yl)-5-methyl-4-oxo-4,5-dihydro-furan-2-carboxylic acid;
5-(4-Bromo-5-methyl-thiophen-2-yl)-5-methyl-4-oxo-4,5-dihydro-furan-2-carboxylic acid;
5-Methyl-4-oxo-5-thiophen-3-yl-4,5-dihydro-furan-2-carboxylic acid;
5-(4-Fluoro-phenyl)-5-methyl-4-oxo-4,5-dihydro-furan-2-carboxylic acid;
5-Methyl-4-oxo-5-pyridin-3-yl-4,5-dihydro-furan-2-carboxylic acid;
5-Ethyl-4-oxo-5-phenyl-4,5-dihydro-furan-2-carboxylic acid;
5-(2-Fluoro-phenyl)-5-methyl-4-oxo-4,5-dihydro-furan-2-carboxylic acid;
2-Methyl-3-oxo-2,3-dihydro-[2,2']bifuranyl-5-carboxylic acid;
5-(3,4-Difluoro-phenyl)-5-methyl-4-oxo-4,5-dihydro-furan-2-carboxylic acid;
5-(2,4-Difluoro-phenyl)-5-methyl-4-oxo-4,5-dihydro-furan-2-carboxylic acid;
5-(2,6-Difluoro-phenyl)-5-methyl-4-oxo-4,5-dihydro-furan-2-carboxylic acid;
5-(2,5-Dichloro-phenyl)-5-methyl-4-oxo-4,5-dihydro-furan-2-carboxylic acid;
5-(3-Methoxy-phenyl)-5-methyl-4-oxo-4,5-dihydro-furan-2-carboxylic acid;
5-Methyl-4-oxo-5-m-tolyl-4,5-dihydro-furan-2-carboxylic acid methyl ester;

5-(3-Ethyl-phenyl)-5-methyl-4-oxo-4,5-dihydro-furan-2-carboxylic acid methyl ester;

5-Cyclohex-1-enyl-5-methyl-4-oxo-4,5-dihydro-furan-2-carboxylic acid methyl ester;

5-(3,5-Dichloro-phenyl)-5-methyl-4-oxo-4,5-dihydro-furan-2-carboxylic acid methyl ester;

5-(3,5-Dichloro-phenyl)-5-methyl-4-oxo-4,5-dihydro-furan-2-carboxylic acid;

5-(3-Iodo-phenyl)-5-methyl-4-oxo-4,5-dihydro-furan-2-carboxylic acid methyl ester;

5-Cyclopentyl-5-methyl-4-oxo-4,5-dihydro-furan-2-carboxylic acid methyl ester;

5-Cyclopentyl-5-methyl-4-oxo-4,5-dihydro-furan-2-carboxylic acid;

5-(3-Cyano-phenyl)-5-methyl-4-oxo-4,5-dihydro-furan-2-carboxylic acid methyl ester;

5-(3-Cyano-phenyl)-5-methyl-4-oxo-4,5-dihydro-furan-2-carboxylic acid;

5-Methyl-4-oxo-5-[3-propenyl)-phenyl]-4,5-dihydro-furan-2-carboxylic acid;

5-(4-Bromo-5-methyl-thiophen-2-yl)-5-methyl-4-oxo-4,5-dihydro-furan-2-carboxylic acid methyl ester;

5-Biphenyl-3-yl-5-methyl-4-oxo-4,5-dihydro-furan-2-carboxylic acid;

5-[3-Hex-1-enyl)-phenyl]-5-methyl-4-oxo-4,5-dihydro-furan-2-carboxylic acid;

5-Methyl-5-(4-methyl-thiophen-2-yl)-4-oxo-4,5-dihydro-furan-2-carboxylic acid methyl ester;

5-Methyl-4-oxo-5-(3-vinyl-phenyl)-4,5-dihydro-furan-2-carboxylic acid;

5-Methyl-5-(4-methyl-thiophen-2-yl)-4-oxo-4,5-dihydro-furan-2-carboxylic acid;

5-Methyl-5-(5-methyl-thiophen-3-yl)-4-oxo-4,5-dihydro-furan-2-carboxylic acid; and

4-Oxo-5-phenyl-5-trifluoromethyl-4,5-dihydro-furan-2-carboxylic acid; or

a pharmaceutically acceptable salt, hydrate or solvate thereof.

23. (previously presented) The compound according to claim 1 wherein said compound is essentially the R enantiomer.

24. (previously presented) The compound according to claim 1 wherein said compound is essentially the S enantiomer.

25. (previously presented) A pharmaceutical composition comprising a compound according to any one of claims 1 and 17 to 24 in combination with a pharmaceutically acceptable carrier.

26. (original) A pharmaceutical composition according to claim 25 further comprising an agent selected from the group consisting of α-glucosidase inhibitor, aldose reductase inhibitor, biguanide, HMG-CoA reductase inhibitor, squalene synthesis inhibitor, fibrate, LDL catabolism enhancer, angiotensin converting enzyme inhibitor, insulin secretion enhancer and thiazolidinedione.

27. (previously presented) A method of treatment of a metabolic-related disorder comprising administering to an individual in need of such treatment a therapeutically-effective amount of a compound according to claim 1.

28. (original) The method according to claim 27 wherein said metabolic-related disorder is selected from the group consisting of dyslipidemia, atherosclerosis, coronary heart disease, insulin resistance, obesity, impaired glucose tolerance, atheromatous disease, hypertension, stroke, Syndrome X, heart disease and type 2 diabetes.

29. (original) The method according to claim 27 wherein said metabolic-related disorder is selected from the group consisting of dyslipidemia, atherosclerosis, coronary heart disease, insulin resistance and type 2 diabetes.

30. (original) The method according to claim 27 wherein said metabolic-related disorder is atherosclerosis.

31. (previously presented) A method of modulating a RUP25 receptor comprising contacting said receptor with a compound according to claim 1.

32. (previously presented) A method of modulating a RUP25 receptor for the treatment of a metabolic-related disorder in an individual in need of such modulation comprising contacting said receptor with a therapeutically-effective amount of a compound according to claim 1.

33. (previously presented) The method according to claim 32 wherein said compound is an agonist.

34. (original) The method according to claim 33 wherein said agonist is a partial agonist.

35. (previously presented) A method of raising HDL in an individual comprising administering to said individual a therapeutically-effective amount of a compound according to claim 1.

36.- 47. (canceled)

48. (previously presented) A method of producing a pharmaceutical composition comprising admixing a compound according to claim 1 and a pharmaceutically acceptable carrier.